REMARKS

Support for the amendments to the claims is shown in the following table:

CLAIM	SPECIFICATION SUPPORT
Claim 11.	Page 2, starting 8 lines from the bottom and starting 4 lines from the bottom.
Claim 12.	Original claim 2.
Claim 13.	Original claim 3.
Claim 14.	Original claim 5.
Claim 15.	Original claim 4.
Claim 16.	Original claim 7.
Claim 17.	Original claim 8.

Accordingly, no prohibited new matter has been added and entry of the new claims is respectfully requested.

I. Summary of the Office Action

The inventions of Groups I and II have been rejoined, no election of species is required.

Claims 9 and 10 are withdrawn from consideration as being drawn to a non-elected invention.

The restriction has been made final.

The Abstract of the Disclosure stands objected to in view of MPEP §608.01(b).

Claims 1, 2, 4, 7 and 8 stand rejected under 35 U.S.C. §112, second paragraph, as allegedly being indefinite.

Claims 1 and 8 stand objected for alleged informalities.

The specification stands objected to as allegedly failing to provide proper antecedent basis for the claimed subject matter.

Claims 1-3 stand rejected under 35 U.S.C. §102(b) as allegedly being anticipated by Nanney et al.

Claims 2, 5, and 6 stand rejected under 35 U.S.C. §102(e) as allegedly being anticipated by Hersch et al.

Claims 1-3 and 8 stand rejected under 35 U.S.C. §103(a) as allegedly being obvious over EP0339905.

Claims 4 and 7 stand rejected under 35 U.S.C. §103(a) as allegedly being obvious over Nanny et al. or EP0339905 further in view of Phan et al.

Claim 3 stands rejected under 35 U.S.C. §103(a) as allegedly being obvious over Hersch et al.

II. Summary of the Response

Claims 1-8 have been cancelled and new claims 11-17 have been added to more clearly describe the invention.

Applicant traverses the restriction requirement because, while the Examiner

alleges that original claims do not use EGF, the art to be searched for proper examination of claims 9-10 would necessarily include EGF. Thus, the search for the subject matter of claims 9 and 10 would be coextensive with a search for the subject matter of claims 1-8. As such, there would be no undue search burden on the Examiner. Applicant, again, respectfully requests that the subject matter of claims 9 and 10 be rejoined with that of new claims 11-17.

Further, Applicant has provided an amended Abstract which conforms to the standards as outlined in MPEP §608.01(b).

The objection to the specification is traversed because the claims are considered part of the specification, as stated in Heide v. Boone, 146 F.3d 1348, 47 USPQ 1128 (Fed. Cir. 1998).

> "The claims as filed are part of the specification and may provide or contribute to compliance with §112, See Northern Telecom v. DataPoint Corp. . . . (Fed. Cir. 1990); In re Benno . . . (Fed. Cir. 1995); In re Frey, . . . 166 F.2d 572,575, 77 USPQ 116, 119 (CCPA 1948)."

As such, Applicant asks that the request to amend the specification in view of the original claimed subject matter be held in abeyance until such a time as the claims are in condition for allowance.

With respect to the rejections as recited in the Office Action, Applicant traverses said rejections against the original claims 1-8 (now cancelled) and explains why the rejections do not apply to claims 9-17.

III. Objection to Claims

Claims 1 and 8 stand objected to because of alleged informalities.

While not acquiescing to the reasons put forward by the Examiner, and to expedite prosecution toward allowance, Applicant has cancelled claims 1 and 8. Therefore, the rejection, as applied against said claims 1 and 8, should be withdrawn as moot.

Further, the objectionable language does not appear in the claims 9-17. Therefore, the objection does not apply against said claims 9-17.

IV. Rejections Under 35 U.S.C. §112, Second Paragraph

Claims 1, 2, 4, 7 and 8 stand rejected under 35 U.S.C. §112, second paragraph, as allegedly being indefinite.

While not acquiescing to the reasons put forward by the Examiner, and to expedite prosecution toward allowance, Applicant has cancelled claims 1, 2, 4, 7 and 8. Therefore, the rejection, as applied against said claims 1, 2, 4, 7 and 8 should be withdrawn as moot.

Further, claims 9-17 possess the necessary positive process steps such that one of skill in the art would understand the metes and bounds of the claimed subject matter.

For these reasons, Applicant submits that the rejection does not apply to said claims 9-17.

V. Rejections Under 35 U.S.C. §102

A. Claims 1-3 stand rejected under 35 U.S.C. §102(b) as allegedly being anticipated by Nanny et al.

Claims 1-3 have been cancelled, thus, the rejection as it might apply against said claims should be withdrawn as moot.

Applicant also explains why the reference does not apply to claims 9-17 for the reasons below.

Nanney et al. do not reveal a method for the treatment of psoriasis in a patient which is a human being. Rather, immunocompromised animals, namely athymic mice are used, whereby psoriatic human lesions are grafted thereupon. This is a very artificial environment which does not allow any conclusions on whether the particular method would also be applicable to human beings. Given the artificial character of the nude mouse model, it is not apparent that this particular model is recognized as correlating to a specific condition.

The model used by Nanney et al. is only one of many different models which have been proposed, but not accepted, as representing the human condition.

In pharmaceutical development the availability of a representative and reliable model is one of the most important contributors toward the successful development of drugs. Without a good and broadly accepted model, it is difficult to decide which lead molecule to put into clinical development.

The need for models which reflect the clinical situation cannot be overstated.

Conversely, without a good model, it is extremely risky and expensive to choose a treatment based only on inaccurate correlations.

Such is the situation in psoriasis. Many models have been proposed (see below), but none is good enough for the pharmaceutical industry to trust. That is the reason why, for example, EGF products have not been clinically evaluated, because results like those disclosed in Nanney et al. have simply not been convincing.

The following is a non-comprehensive list mentioning a few examples of models from the recent literature:

- Use of leukotriene B4 as a measure of degree of psoriasis
- An in-vitro model based on an IFN-gamma/ K17 autoimmune loop (Bonnekoh et al; 2001)
- The use of HaCaT cell line as an in-vitro model system (also related to the INF-gamma overexpression)
- An in-vitro model of human T-cell transmigration (Li et al; 2003)
- An in-vitro model based on angiogenesis using human endothelial cells (H. Schmidt et al; 2003)
- A cell-free system from slime molds to measure the effect of Vitamin D3 on ribonuclease P.
- Transgenic mice which express suprabasal integrin in the epidermis (JM Carroll et al; Cell 1995)

Apart from those examples, persuasive evidence that a reasonable animal model for psoriasis was missing at the priority date of the present application can be taken from Jackson M et al. (The FASEB Journal. 1999; 13:495-502) where it is stated:

"The factors involved in triggering and maintaining the chronic plaque of psoriasis remain undetermined, since no adequate animal or *in vitro* model exists with which to test them directly. Current therapies available for psoriasis reduce the symptoms of the disease, which often recurs once treatment ceases. An understanding of mechanisms underlying psoriasis immunopathogenesis is therefore of great importance for the development of more effective and specific treatments."

The clinical evaluation by the present inventor was carried out successfully with human subjects and represents a direct correlation with the naturally occurring disease state. No other previous model could have removed all uncertainty about the use of EGF in psoriasis.

As such, the Nanney et al. reference is not enabling for claims directed to treatment of human subjects, and thus, is an ineffective reference as to the claimed invention.

For these reasons, Applicant respectfully submits that the rejection does not apply to claims 9-17.

B. Claims 2, 5 and 6 stand rejected under 35 U.S.C. §102(e) as allegedly being anticipated by Hersch et al.

Claims 2, 5 and 6 have been cancelled, and thus, the rejection as it might apply against said claims should be withdrawn as moot.

Hersch et al. do not disturb the patentability of claims 9-17 for the reasons below.

Hersh et al. is not related to a method for the treatment of psoriasis but to the treatment of ultraviolet radiation skin damage.

The only passage where psoriasis is mentioned in Hersch et al. is in column 9, line 28. However, only selenium is disclosed as being used as the sole active agent. Thus, Hersch et al. does not teach the use of EGF in patients with psoriasis.

Therefore, the particular combination as described by Hersh et al. of several pharmaceutically active ingredient is different from what is the subject of the pending claims.

For these reasons, Applicant respectfully submits that the rejection does not apply to claims 9-17.

VI. Rejections Under 35 U.S.C. §103(a)

A. Claims 1-3 and 8 stand rejected under 35 U.S.C. 103(a) as allegedly being obvious over EP0339905.

Claims 1-3 and 8 have been cancelled, thus, the rejection as it might apply against said claims should be withdrawn as moot.

EP 0339905 does not apply to claims 9-17 for the reasons given below.

EP 0339905 clearly teaches the use of a pharmaceutically acceptable chemical entity which is capable of increasing the number of receptors for the growth factor on the membranes of cells at a wound site in connection with a polypeptide growth factor having mitogenic or angiogenic activity. The latter polypeptide growth factor can, among others, be EGF, whereas the chemical entity is, e.g., a retinoid. From this it is clear that the subject matter of this European patent application is not related to a method for the treatment of psoriasis using EGF. On the contrary, the mode of action of the EGF as

used in connection with the present invention is to down-regulate the expression of the EGF-receptor. Therefore, EP0339905 clearly teaches away from the subject matter of the present application.

As one of skill in the art would not expect to successfully achieve the invention as claimed in view of the cited reference, the claims 9-17 are not obvious over EP0339905.

B. Claims 4 and 7 stand rejected under 35 U.S.C. 103(a) as allegedly being obvious over Nanney et al. or EP0339905 in view of Phan et al.

Claims 4 and 7 have been cancelled. Thus, the rejection as it may apply against said claims should be withdrawn as moot.

The combination of references does not apply to claims 9-17 for the reasons given below.

With respect to Nanney et al., as stated above, said reference is not enabling for the treatment of human subjects. Further, according to the holdings in Beckman Instruments, Inc. v. LKB Produkter AB, 892 F. 2d 1547, 13 USPQ2d 1301 (Fed. Cir. 1989):

> "In order to render a claimed apparatus or method obvious, the prior art must enable one skilled in the art to make and use the apparatus or method."

Also, that there is still a need for an effective compound or pharmaceutical formulation for the treatment of psoriasis confirms that despite the animal models used for basic research in relation to psoriasis, neither the particular system used by Nanney et al. nor the results obtained therewith were convincing to persons skilled in the art and thus were not suitable to satisfy the long felt need for the particular use of an EGF

containing formulation. In other words, in view of the athymic mouse model, one skilled in the art would not have expected EGF to be used as a pharmaceutically active compound in the treatment of psoriasis in humans.

The deficiency identified in Nanney et al. is not cured by the teachings of Phan et al.

Phan et al. describe the use of sulfadiazine for the treatment of patients suffering from psoriasis and pyoderma gangrenosum. However, there is no mention in Phan et al. to use EGF for that purpose either alone or in combination with sulfadiazine.

Thus, there is no motivation to combine the teachings of the references and accordingly, a prima facie case of obviousness has not been made.

With respect to EP0339905, the reference envisages the use of EGF with retinoids or equivalents thereof. Again, the new claims as recited use EGF alone or in combination with non-retinoid anti-inflammatory agents. As such, there is no suggestion from the teachings of EP0339905 to use EGF alone to treat psoriasis.

Further, given the fact that in contrast to the down-regulation which is intended by the administration of EGF in the practice of the instant invention, EP0339905 teaches the use of compounds which do exactly the opposite, namely to provide further compounds which increase the expression of the EGF receptor.

Again, Phan et al. does not cure the deficiencies identified in the primary reference.

Thus, there is no motivation to combine the teachings of the references and a prima facie case of obviousness has not been made. Even if combined, the aggregate

teachings are disparate from the claimed invention, in fact are incompatible with the teachings of EP 0339905, for example increasing EGFR rather than decreasing EGFR as found in the practice of the instant invention. One of skill in the art would have no reasonable expectation of successfully achieving the invention as claimed.

For these reasons, Applicant respectfully submits that the rejection does not apply to claims 9-17.

C. Claim 3 stands rejected under 35 U.S.C. §103(a) as allegedly being obvious over Hersch et al.

Claim 3 has been cancelled, thus, the rejection should be withdrawn as moot.

Hersch et al. does not apply to claims 9-17 for the reasons given below.

It would have been impermissible hindsight to abstract from Hersh et al. that the particular technical teaching of using reduced L-glutathione selenium in combination with an epidermal growth factor for the treatment of ultraviolet radiation skin damage would lead one of skill in the art to use one of the respective ingredients described therein, namely EGF, as the sole active ingredient for the treatment of human beings suffering from psoriasis.

Further, the particular formulation according to the new claims does not comprise a combination of glutathione and selenium. In addition, as outlined above, Hersh et al. does not describe the use of the particular combination, which is different from the subject matter of the new claims for the treatment of psoriasis. Therefore, using a composition which only comprises a part of the ingredients of the composition according to Hersh et al. for the treatment of a human being suffering from psoriasis would not be

obvious in view of Hersh et al.

Therefore, one of skill in the art would not have a reasonable expectation of successfully achieving the invention as claimed.

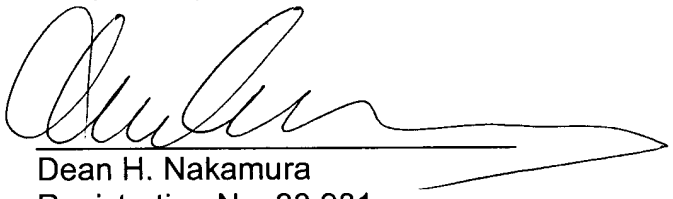
Accordingly, Applicant submits that the rejection does not apply to new claims 9-17.

CONCLUSION

Applicant submits that the pending claims are in condition for allowance. Reexamination, reconsideration, withdrawal of the objections and rejections, and early indication of allowance are requested respectfully. If any questions remain, the Examiner is urged to contact the undersigned at the local exchange noted below.

If any fees are found to be applicable, please charge any additional fees or make any credits to Deposit Account No. 07-1896.

Respectfully submitted,



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ABSTRACT

Topical agent formulations for the treatment of psoriasis containing epidermal growth factor (EGF).